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PCT/JP2004/003334

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference C1-A0303P	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/JP2004/003334	International filing date (*day/month/year*) 12 March 2004 (12.03.2004)	Priority date (*day/month/year*) 13 March 2003 (13.03.2003)
International Patent Classification (IPC) or national classification and IPC C07K 16/28, A61K 39/395, A61P 7/00, 7/04, G01N 33/15, 33/50		
Applicant CHUGAI SEIYAKU KABUSHIKI KAISHA		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I — Basis of the report
- ☐ Box No. II — Priority
- ☒ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

Date of submission of the demand 12 March 2004 (12.03.2004)	Date of completion of this report 02 May 2005 (02.05.2005)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ The international application as originally filed/furnished

☐ the description:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

pages _____, as originally filed/furnished

pages* _____, as amended (together with any statement) under Article 19

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the drawings:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 16, 17

because:

☒ the said international application, or the said claims Nos. 16, 17 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

The inventions of claims 16 and 17 concern a method for treating a disease. This corresponds to a method for treating an animal or human body by therapy, which does not require a preliminary examination by the International Preliminary Examining Authority.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 16, 17.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ see Supplemental Box for further details.

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Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	5-9, 13-15, 18-29	YES
	Claims	1-4, 10-12	NO
Inventive step (IS)	Claims		YES
	Claims	1-15, 18-29	NO
Industrial applicability (IA)	Claims	1-15, 18-29	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Document 1: US 2002/0193571 A1 (CARTER P J et al) December 19, 2002 (Family: none)
Document 2: JP 2001-506135 A (Abbott Laboratories) May 15, 2001 & WO 98/28331 A2 & EP 946726 A2 & MX 9905856 A1 & US 2001/0006796 A1 & US 6323000 B2, & US 2003/0073161 A1 & US 6683157 B2
Document 3: Ballmaier M. c-mpl Mutations are the cause of congenital amegakaryocytic thrombocytopenia, Blood, 2001, Vol. 97, No. 1, p. 139-46
Document 4: JP 2001-513999 A (Genentech, Inc.) September 11, 2001 & WO 99/10494 A2 & AU 9888312 A & EP 1009831 A2 & US 6342220 B1 & AU 755822 B

Claims 1-4 and 10-12

Document 1 describes an agonist antibody to a mutant WSX receptor, and therefore this examination finds that document 1 describes the inventions of claims 1-4 and 10-12.

In addition, with respect to the "agonist" of claim 1, the agonists that are supported in the Description in the sense of PCT Article 6 and fully disclosed in the sense of PCT Article 5 are only antibodies and constitute only a small part of the claimed compounds.

The same applies to the inventions of claims 3-7, 10, 12-15, 23, 24, 26-29, and the "substance obtained by the screening method" of claim 22.

As a result, a search was conducted only on items that are supported and fully disclosed in the Description, i.e., the antibodies. In addition, a complete search was conducted for the inventions of claims 2, 8, 9, 11, 18-21, and 25.

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. 1, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis that of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☐ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☐ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purpose of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

** If item 4 in Box No. I applies, the listing and /or table(s) related thereto, which form part of the basis of the report, may be marked "superseded".*

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of Box V:

Claims 1-15 and 18-29

Document 2 describes a mutant human α7 acetylcholine receptors subunit among nicotinic acetylcholine receptors; it states that mutant receptors include both those that increase activity and decrease activity; it states that when identifying compounds that modulate acetylcholine receptor activity, there may be compounds that are agonists or antagonists toward mutant receptors; and it describes the preparation of cells expressing mutant receptors and the evaluation of the ability of test compound to elicit a suitable response (document 2, page 25, line 12 to page 26, line 8). In addition, document 2 states that spontaneous mutations in neuron acetylcholine receptors may bring about the death of specific groups of neurons; it states that it is possible to use the mutant receptor to screen for compounds that express a cytoprotective effect; it states that the mutants can be used to select agonists or antagonists from among ligands to screen for compounds that will be useful for treating various disorders; and it describes the identification of cytoprotective compounds that mutually interact with the mutant acetylcholine receptors based on the knowledge that activation of the α7 acetylcholine receptor subunit is cytoprotective (document 2, page 26, line 9 to page 29, line 25).

Document 3 states that congenital amegalokaryocytic thrombocytopenia (CAMT) occurs when transduction of the thrombopoietin (TPO) signal does not occur due to an amino acid mutation in the TPO receptor.

Document 4 describes agonist antibodies to the TPO receptor, and it lists an antibody fragment, single stranded antibody, a diabody, etc., as antibodies (document 4, Par. Nos. 0029 and 0064 to 0069). In addition, it states that the agonist antibodies can stimulate the propagation of hemopoietic cells and can be used for the treatment of thrombocytopenia, etc. (document 4, Par. No. 0155).

Because document 2 describes the screening of agonists of a mutant receptor, the activation of the receptor, and the use thereof in the treatment of disorders, this examination finds that persons skilled in the art can easily conceive of preparing an agonist as described in document 2 to transduce a mutant TPO receptor signal, which is the cause of the disease described in document 3.

In addition, this examination finds that persons skilled in the art can select agonists that have higher agonist activity than naturally occurring ligands, select the agonist antibodies described in document 4, and select low molecular weight antibodies and diabodies as the types of antibodies.

As a result, this examination finds that persons skilled in the art can easily prepare the inventions of claims 1-15 and 18-29 based on the descriptions in documents 2-4.